Depression is a common disease

Major depressive disorder is a severe clinical and economic burden striking 10 to 15% of the population at some time. At any given year around 4% of the population is affected by a depressive episode which recurs on average six times per lifespan. The dimension of the problem is reflected by 1 million cases of suicide per year worldwide and the increased risk among depressives for coronary heart disease, dementia and diabetes.

Current status of antidepressant therapy

First line treatment for severe-to-moderate depression are antidepressants that vary in the extent to which they interfere with different neurotransmitter processes in the brain. In the absence of knowledge which causal factors account for the disease in the individual patient a trial-and-error schedule remains the only option. As a consequence around 30 to 50% of patients do not respond to the first antidepressant medication. Relapse into a subsequent depressive episode is more frequent among responders (improvement in severity of symptoms by more than 50%) than among remitters that are symptom-free. Therefore, remission but not response is the aim in clinical depression care. Unfortunately, less than 40% of patients remit with commonly used antidepressants despite long treatment periods.

ABCB1 gene and the blood-brain barrier

The brain tissue is protected from potentially harmful molecules in the blood circulation by the blood-brain barrier. A central role is played by the "custodian molecule" P-glycoprotein (P-gp) that is encoded by the ABCB1 gene. It is located at the interface between blood vessels and brain cells. There it complicates antidepressant therapy as about 70% of all common antidepressants are recognized by P-gp that impedes their penetration into the brain. A drug that is recognized by P-gp is called substrate and if not recognized the drug is a non-substrate. It was shown that ABCB1 gene variants influence the function of the P-gp and by this route they determine the clinical effect of the antidepressant (Uhr et al 2008).

Figure 1: Schematic illustration of the P-gp mechanism at the blood-brain barrier

Personalized antidepressant treatment

Before initiation of an antidepressant therapy analysis of the ABCB1 genotype is highly recommended. The ABCB1 gene carries a number of variants with unequal impact on clinical outcome. Researchers at the Max Planck Institute of Psychiatry have identified two variants that are best suited to discriminate between favorable and less favorable ABCB1 genotypes with respect to antidepressant treatment outcome. These variants are patent protected for this specific use and implemented in the commercially available RIDA®PRECISION ABCB1 test. The test result advises the doctor which antidepressants should be administered at which dose. Many clinical studies corroborated that antidepressant treatment guided by the ABCB1 test is superior to "treatment-as-usual". If the clinically effective antidepressant is chosen a more rapid onset of action and higher remission rates can be expected (Breitenstein et al 2014; Sarginson et al 2010).
Recommended treatment schedule based on the ABCB1 test result

In case the ABCB1 test result identifies the patient as carrier of gene variant 1 (around 25% of all patients) a beneficial treatment outcome can be expected if two requirements are fulfilled: (1) The antidepressant is a P-gp substrate; and (2) The administered dose results and plasma drug concentrations within the recommended limits. Patients with gene variant 2 (around 75% of the patients) where P-gp is more effectively including response require a more intense treatment plan. In this case the options are: (1) increasing the dosage of the P-gp substrate; (2) Switch to administration of a non-substrate; and (3) Augmentation using anticonvulsants, lithium or atypical antipsychotics and psychotherapy.

Just a few steps to treatment recommendation

If the treating doctor wants to be informed about his patients ABCB1 genotype the following steps must be heeded:

1) The doctor explains the advantage of an ABCB1 test guided antidepressant treatment.
2) Together with his patient the doctor fills out the order form for the RIDA® PRECISION ABCB1 test.
3) The doctor collects a blood sample.
4) The sample is sent to a laboratory offering the RIDA® PRECISION ABCB1 test.
5) The laboratory conducts the RIDA® PRECISION ABCB1 test by analysis of the DNA extracted from the patient’s leucocytes.
6) Within a few days the test results will be sent to the treating doctor together with recommendations.
7) The informed doctor is now able to tailor the therapy according to the patients ABCB1 test result.

For further information please visit: www.abcb1-test.de

Benefits of RIDA® PRECISION ABCB1 test

- Swifter choice of the right drug
- More effective treatment
- Higher remission rate
- Performed quickly and easily
- Less side effects
- Only one single test needed
- Favorable cost/benefit ratio
- Profiting from leading edge clinical science

Most important issues at a glance

- Antidepressant therapy is unsatisfactory as even treatments as long as several months often fail to achieve remission.
- The ABCB1 test predicts which antidepressants are best suited for the individual patient. That applies for initial treatment and for a switch in therapy.
- The ABCB1 test result leads to recommendations from which antidepressants and supporting measures the individual patient will benefit most. The ABCB1 test guided antidepressant therapy helps to achieve the best possible clinical outcome and increases the chance of full remission.

Figure 2: Treatment schedule based on ABCB1 test result

Examples for P-gp substrate are Paroxetine, Citalopram, Escitalopram, Venlafaxine, Amitriptyline, Amtriptylinoxde, Nortriptiline, Trimipramine and Vortioxetine. Examples for P-gp Non-substrates are Fluoxetine, Mirtazapine and Agomelatine.